Acute toxicity study on ARTHA GO capsules by using wistar rats

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ABSTRACT

The aim of this study was to investigate the acute toxicity of ARTHA GO capsule using Wistar rat. Acute toxicity study was performed using OECD guidelines 421, a dose of (5mg/kg, 50mg/kg, 300mg/kg or 2000mg/kg) body weight administered orally to rats. In this study daily for 14 days animals were observed for toxic symptoms and mortality are subjected to necropsy; the animals which are intercurrently scarified also the one survive until the end of test are subjected to necropsy. Change in body weight, water intake, food intake as well as cage side observation were observed and reported in this study. The result of this acute toxicity study neither signs of toxicity nor mortality among the rats were observed of the experimental period. The overall this acute toxicity study indicates that ARTHA GO capsules is non-toxic up to a dose of 2000mg/kg body weight, which could be considered a safe dose.

Keywords: herbal formulation, inflammation, acute toxicity, capsule, arthritis, ARTHA GO

1. INTRODUCTION

Herbal medicine is extensively practiced in the prevention, diagnosis; treatment of various illnesses [1]. Toxicity is the science of poisons. In acute toxicity study the organization for economic and development mentioned as the advance effect occurring within a short time of

oral route of administration of a simple dose of substance or a multiple doses given within 24 house, for the interaction of poisons leads to injury or death of living tissue. In herbal medicinal plants ancient human categorized some as safe plants and some as harmful [2].

ARTHA GO capsule is herbal formulation which commonly has anti-inflammatory activity [6]. Also it is useful for relieving pain and Arthritis. Capsules are oral delivery of therapeutic compounds which alternative to tablets available as hard as well as soft shells and capsules are formulated from a non-gelatin or gelatin polymeric material [3]. ARTHA GO capsules are also useful for any disorder that affects joints. Arthritis includes joint pain and stiffness and other may include warmth, swelling, and also decreased range of motion of the affected joints. Rheumatoid arthritis and spondyloarthritis are two common types [4]. In the herbal formulation of ARTHA GO capsule various types of herbs are used like; Sunthi: Zingiber officinale belonging to family zingiberaceae. It is commonly used actions like antiemetic, stomachic, expectorant, anti-inflammatory, aphrodisiac etc [5].

Pipali: Piperlongum belonging to family piperaceae. Pharmacological activities of pipali are antibacterial, anti-tumour, anti-allergic etc [7]. Chitrak: It is a dried natural root of plumbago zeylanica family plumbaginaceae. Pharmacological activities like anti-allergy, anti-inflammatory, anti-cholesterol, anticancer, anti-oxidant etc [8]. Guduchi: it is a large, glaborous shrub family menispermaceae [9]. Nirgundi: it is natural flexible stem belonging to family verbenaceae [11]. Gokhru: belonging to family Zygophyllaceae used for analgesic, anti-inflammatory, antibacterial, antispasmodic activity [10]. Erandmool: belonging to family Ephorbiaceae it used for anti-inflammatory activity, antiulcer, laxative, pergavtive [12]. punarnava: belonging to family Nyceaginaceae [13], GandhPrasarini, suddhGugal, Chopchini this also are important herbs used in ARTHA GO capsule. This article based on to determine the toxicity of ARTHA GO capsule.

2. MATERIALS AND METHODS

Animals

Healthy Wistar Albino rats weighing in range 130 – 170 gms, the animal were housed in 37cm*23cm*16cm* polypropylene cages with five rats in one cage and the cage were placed in limited-access premises of animal house with control temperature and humidity. Animals obtained from the Central animal house Preclinical Research Facility, Datta Meghe Institute of medical sciences, Sawangi (Meghe), wardha, Maharashtra (india). Non pregnant female Wistar Albino rats were used for acute toxicity study. Food was provided by standard feed prepared and plain tap water were provided ad libitum. The artificial lighting ensured a sequence of 12 hour light and 12 dark. Animal were acclimatized for 7 days in laboratory conditions before the experiments.

Drug

The supplier provided the test drug containing medicinal herb as ARTHA GO CAPSULE. This herbal medicine ARTHA GO capsules, manufactured by Gayatri Ayur pharma Pvt.Ltd. 234/2/2, patelested, Nikol Road, Ahmdabad, Gujrat (India), 382350. The substance was stored in at ambient temperature and out of the light. This formulation various herbs are used like sunthi (zingiber offcinale) 60mg, pipali (piper longum) 30mg, chitrak (plumbago zeylanica) 20mg, chopchini (smilax china) 50mg, suddhgugal (balsamodendron mukul) 40mg, gokhru (tribulus terrestris) 50mg, guduchi (tinsopora cordifolia) 50mg, nirgundi (vitex negundo) 50mg, errand mool (ricinus communis) 60mg, punarnava (boerhaavia diffusa) 40mg, gandh prasarini (paeseria foetida) 50mg [15].

Acute toxicity study

Wistar albino female rats of weighing between 130-170gm maintained under standard laboratory conditions were used for acute toxicity study. This selection based according to the Organization for Economic Cooperation and Development (OECD) guideline 421. Total 5 female wistar rats were selected for the study. Animals were kept overnight fasting prior to drug administration. Food provided after 3-4 hour of dosing. Observation was daily for next 14 days for every 24 hours and daily observation on the change in weight, skin, eye, mucus membrane and nervous system [15-17].

Protocol:

1	Animal species	wistar albino rat
2	Sex	female
3	Body weight	130-170 gms
4	Animal per group	5
5	No of doses group	1
6	Route of administration	oral route

7	Vehicle of administration	distilled water
8	Observation period	14 days

Experimental deign

Preparation of test substance:

The test substance ARTHA GO capsule was triturate and suspended in water using 1% gum acacia as a suspending agent and 0.1% tween 80 as a wetting agent.

Administration of test substance:

All animals were weighed again before drug administration and animal fasted overnight prior to the test substance administration. The volume per 100gm of body weight, defined to 2 ml/100gm, the volume to administer was calculated for each rat. The test substance was administered in a single dose orally by using a syringe fitted with suitable size canualla, after administration, animals were fasted for 3-4 hours.

Selection of dose

The starting dose of test substance was selected as 2000mg/kg it was an Ayurvedic medicine.

Statistical analysis

In this toxicity study experimental results are expressed as means ± SD [14].

3. CLINICAL OBSERVATION

The stage of dosing to the end of study animals was carried out by general observations on daily basis. The clinical observation made individual, every animal was examined outside the home cage. Animals were observed individually after dosing during first 30mins, periodically during the first 24 hours and daily thereafter of 14 days. The different types of parameters were observed – changes in skin and fur, eyes and mucus membrane, respiratory function, tremors, convulsions, salivation, diarrhea, lethargy, sleep and coma. The clinical observation detailed below under investigation:

1	Condition of fur	Normal
2	Damage area of skin	Normal
3	Abnormal detension	Normal
4	Eye dullness	Normal
5	colour and condition of faeces	Normal
6	Condition of teeth	Normal
7	Breathing abnormalities	Normal
8	Eye opacity	Normal
9	Sleep condition	Normal

Body weight

Day before administration, then on day 8 and day 15 the animals were weighed regularly i.e.7 and 14 days after administration of test substance.

Pathology

At the end of 14 days all animals surviving of the observation were scarified by intraperitoneal injection of 65 sodium pentobarbital solution at the rate of 12ml/100gm and bled at the femoral artery. They were necropsied and also organs like kidney, liver, heart were examined microscopically [18,19].

4. RESULTS

Acute toxicity study

Single oral administration of ARTHA GO capsule suspension up to dose of 2000mg/kg body weight no any mortality and morbidity or any toxicity or no any sign of behavioural changes observed throughout the 14 days.

Effect on body weight

Throughout the period of 14 days all animals exhibited normal and comparable body weight. There was slightly changes weight of day one and day fifteen was noted. The weight variation of test group was recorded and reported in table I.

Food and water consumption

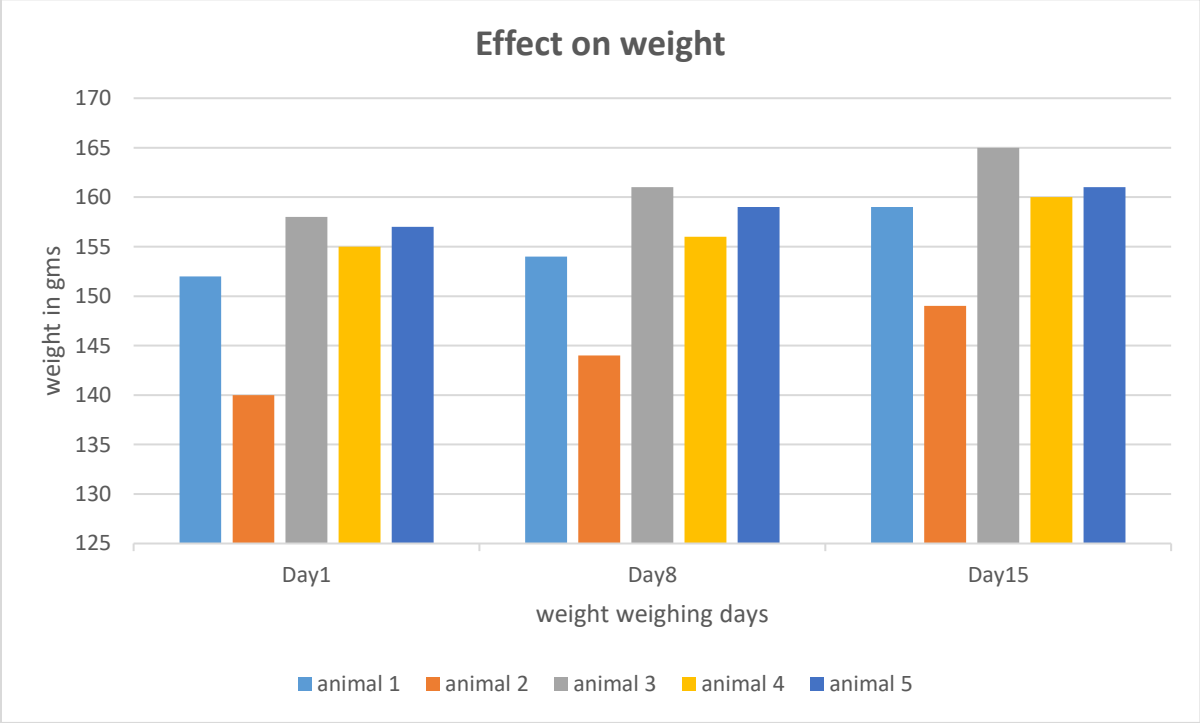
There was no significant change in food and water consumption [14].

Clinical signs

Throughout the acute toxicity study there was no abnormal signs was observed [15].

Table I- changes in body weight at day one, eight and fifteen at a dose of 2000mg/kg

Animal no	Weight in Gm		
	Day 1	Day8	Day15
1	152	154	159
2	140	144	149
3	158	161	165
4	155	156	160
5	157	159	161
Mean	**152.4**	**154.8**	**158.8**
SD	**±7.30**	**±6.61**	**±5.93**



Food and water consumption

There was no significant change in food and water consumption.

Clinical signs

Throughout the acute toxicity study there was no abnormal signs were observed.

Mortality

In assessing the acute toxicity study (LD50) of a drug mortality is main criterion.

Haematological analysis

Blood sample was collected after the compilation of study and it collected in heparinized tube. Parameters evaluated include – RBCs count, WBCs count, platelets, monocytes count, Hb. In 14 days of study the result were shows that no significant changes in haematological parameters.

Histopathology

Necropsy were found normal in all animals. ARTHA GO capsule does not affected the histology of vital organ, viz., kidney, lungs, heart, liver. No any abnormalities were detected in macroscopic examination [17].

Table II Observation table of acute toxicity study

Sr no	parameters	Animals				
		1	2	3	4	5
1	Lacrimation	NO	NO	NO	NO	NO
2	salivation	NO	NO	NO	NO	NO
3	Piloerection	NO	NO	NO	NO	NO
4	Drowsiness	NO	NO	NO	NO	NO
5	Tremors	NO	NO	NO	NO	NO
6	Convulsion	NO	NO	NO	NO	NO
7	Fur	Normal	Normal	Normal	Normal	Normal
8	Food consumption	Normal	Normal	Normal	Normal	Normal
9	Water consumption	Normal	Normal	Normal	Normal	Normal
10	Mortality	NO	NO	NO	NO	NO
11	Histopathology	Normal	Normal	Normal	Normal	Normal

5. DISCUSSION

In this acute toxicity study of herbal product was analyzed in male wistar albino rats. The acute toxicity study was conducted 14 days at the dose of 2000 mg/kg, no any mortality and morbidity was observed. For acute treatment this proves that drug could be safely administered to the dose 2000mg/kg. This study test assesses the adverse effect that occurs within a short time after administration of a single dose of a test substance.

As compared to allopathic formulation and polyherbal formulation are abundantly used in developed countries for treatment of different types of aliments. This formulation was mixture of herbal plant formulated in the form of capsules. These capsules are used in relieving pain and inflammation of joints also prevention from arthritis. The test substance did not produce any signs of toxicity and no any mortality was observed in treated group i.e. 2000mg/kg during the study period. For assessment toxicity study body weight change is an important index, in the present toxicity study, there was a gradual normal increase in mean body weight of the test group. In this study all haematological parameter which was observed show normal. Liver, kidney and other organ of rats are used to assess the safety or toxicity of drugs or plant material. In current toxicity study, pathological examination of the liver and kidneys of test group did not show any major changes in size, shape, colour, and texture. There was no significant difference in the absolute weight of liver and kidneys of test group. Therefore, be considered that this herbal formulation is safe for human also [15, 17].

6. CONCLUSION

Acute toxicity study revealed that this polyherbal formulation is non-toxic with oral dose of 2000 mg/kg. The result support that the herbal formulation ARTHA GO capsule is safe and no deleterious changes were observed in behaviour and habits, hematology and histopathological parameter. The substance ARTHA GO capsules supplied by Gayatri Ayurpharma 234/2/2, Patel Estate, Ahmdabad, 380049 was classified in the hazard category- 5 or unclassified with a LD50 higher than 2000mg/kg in the rat [18,19,20].

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This study has not received any external funding.

Conflict of Interest:
The authors declare that there are no conflicts of interests.

Peer-review:
External peer-review was done through double-blind method.

Data and materials availability:
All data associated with this study are present in the paper.

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